ONCERNING THE INFLUENCE EXERTED BY EACH OF THE CONSTITUENTS OF THE BLOOD ON THE CONTRACTION OF THE VENTRICLE. By SYDNEY RINGER, M.D., Professor of Medicine at University College, London. Plate XIX.

In this paper I record experiments designed to ascertain the influence each constituent of the blood exercises on the contraction of the ventricle.

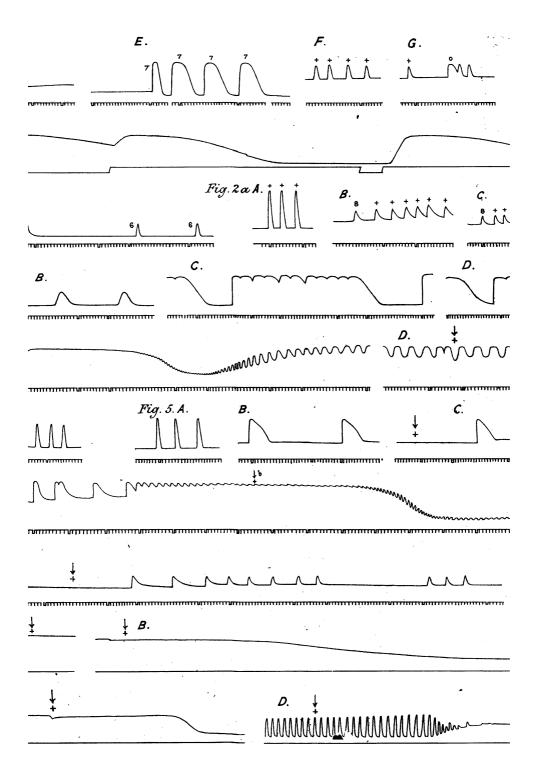
By "saline solution" I mean the ordinary 0.75 per cent. solution of sodium chloride. "Blood mixture" was made from dried bullock's blood dissolved in water to represent normal blood, and this I diluted with five parts of saline solution.

In each experiment I always used 100 c. c. of saline solution or of blood mixture. The tracings were taken with Roy's tonometer, and run from left to right. The experiments were made in April and May. The ventricle was tied on the cannula as nearly as possible in the auriculo-ventricular groove. A figure or \* over the trace indicates that the contraction was excited by faradaic stimulation, the figure showing the position of the secondary coil.

When the circulating fluid consists only of "saline solution" the ventricular beats undergo the following changes (see Fig. O, Oa, 1, 5, 6). The contraction at first becomes more complete if the ventricle empties itself imperfectly. The trace soon becomes broader, its summit rounder (see Fig. O, B), at the same time there is slight diastolic contraction (persistent spasm). Next, the period of relaxation becomes greatly prolonged (see C; Fig. 5, B, and Fig. 6, B), and the whole trace is permanently raised higher above the base line.

During these changes affecting the expansion of the ventricle the contraction is very little altered, being rather accelerated, see Fig. Oa (trace taken with quicker rate), where A shows the trace with blood mixture, B the trace after saline solution was substituted for blood

Journal Physiology, Fig. 0. A. **C**. D. Fig. Oa. A. В. Fig. 2. B. C. Fig. 3. A. Fig. 4. A. C. В. G. F. Fig. 4 a. A. Fig. 6. A. В C. D. Fig. 7. A. C.



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H	
P. + + + + + + + + + + + + + + + + + + +	Fig. 3 a. A. B.  C. D. E.
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mixture. The dip in the abscissa shows the time the make, and the rise the time the break induction shock was delivered. The secondary coil stood at 3. These effects, therefore, are very similar to those produced by veratria.

Next, this prolongation of the ventricular dilatation grows less, at the same time the trace rises still higher above the base line (see Fig. O, D). In a series of contractions excited after a standstill of some 50 or 60 seconds the first contraction dilates more rapidly than the subsequent ones. This is still better seen in E, taken from another experiment.

These changes in the trace increase, that is, the whole trace rises higher and higher above the base line, the amplitude and duration of each contraction grows less, and the dilatation often becomes less prolonged (see F). At the same time the ventricle undergoes another curious change. After the contractions have become weakened the duration of the contraction and the slowness of dilatation are influenced by the strength and duration of the stimulus. For instance, in some cases if, in the case of a ventricle not contracting spontaneously, the coil be moved from, say, 8 to 0, the contraction is prolonged and followed by spontaneous contractions (see G), where the contraction with \* over it was excited with the coil at 8, the contraction with o over it with the coil at zero.

Again, if the faradaic excitations be continued till the trace has nearly completed its rise, the contraction is much prolonged. See H, where the first contraction was excited by a momentary excitation, the connection in the secondary current being made and broken as speedily as possible, and the coil standing at 8. In the second contraction the faradaization was continued to the point opposite the dot, the coil still standing at 8. In the third contraction the coil stood at 0, and the faradaization was continued to the point opposite the dot. The second contraction is much more prolonged than the first, and the third than the second; and, moreover, the third contraction is followed by a series of spontaneous beats. This is still better seen in I, taken from another experiment. In the first series each contraction was excited by the shortest duration of faradaization possible, the secondary current being made and broken as speedily as possible. In the second series of contractions the faradaization was continued to a level with the dot. In each series the coil stood at 7. This effect of an increase in the strength, or duration, and number of stimuli does not occur in a heart fed with blood, nor, in the early stages, with saline. With a stronger solution of sodium chloride—as, for instance, 1.5 per cent.—all the above changes occur earlier.

When the dilatation is greatly prolonged, in many cases the dilatation is completed at the base, whilst the rest of the ventricle remains quite contracted, and then the dilatation extends gradually to the apex. Sometimes, before the dilatation has spread far down the ventricle, the dilated portion contracts again, and there ensues a partial fusion of the excursions in the trace; in fact, we get an imperfect tetanus, the fusion being due, not to increased frequency of the contractions, but to their great prolongation, a second contraction beginning before its predecessor is finished (see Fig. 1, C).

Blood, even in small quantities, obviates the changes with saline solution. Thus fresh or dried blood diluted with three or four parts of saline does not induce the character of contraction occurring with saline, and yet the blood mixture contains as much soda salts as saline solution.

On one occasion I dissolved the dried blood in "saline solution," so that the blood mixture contained an excess of soda salts, and this mixture did not prolong the ventricular dilatation. In other experiments I added to the blood mixture one, two, and three times its own quantity of saline, and with the larger additions only very slightly increased the duration of the contractions. On another occasion I added to the 100 c. c. of saline solution 25 c. c. of blood mixture, and almost entirely removed the effect of the saline, the contractions becoming of much shorter duration, and the dilatation much more rapid.

Blood mixture not only obviates the changes occurring early with sodium chloride, but also the later changes. This effect is seen in Fig. 2a. In about 60 minutes, with saline, the contractions had grown very weak, the dilatation remaining prolonged (see B). On substituting blood for saline, at first the contractions became still weaker, but the dilatation became more rapid. The contractions then slowly improved, and soon the dilatation became as quick as at first, and in about 40 minutes after the saline was changed for blood mixture the contractions had become almost as good as at the beginning of the experiment. On the addition of blood solution, or on replacing saline with blood solution, the contractions at first become much less frequent and weaker (see Fig. 2), but in a short time the contractions became good again.

If sodium chloride is added from time to time to the blood mixture till enough is employed to arrest the ventricle, still we do not produce the character of trace that occurs when the ventricle receives only saline solution. This is well shown in Fig. 3. At A is shown the effects of 5 c. c. of 20 per cent. solution of sodium chloride. This quickly weakened and arrested the ventricle. I then restored contractions by adding 50 c. c. of water to the circulating blood mixture and again weakened the ventricle by adding 2 c. c. of 20 per cent. chloride of sodium solution (see B). I then substituted for the blood mixture saline solution, and got the characteristic saline solution trace, the dilatation becoming greatly prolonged (see C and D). These last tracings will show the effect of a prolongation of the contraction on the production of tetanus, for in C and D there is considerable fusion of the contractions, not by increasing their frequency, but by prolonging the duration of each beat, so that one begins soon after its predecessor is nearly completed.

In Fig. 3a I give the effect of repeated smaller additions of sodium chloride solution to the blood mixture, and it will be seen that, administered in this way, we do not produce the change that occurs with simple saline solution. Blood, then, obviates the changes occurring in the contractions of a ventricle receiving only saline solution, and the question arises, Which constituent of the blood has this property?

I find that a small quantity of white of egg completely obviates the changes occurring with saline solution. I first took tracings with blood mixture; I then replaced the blood with 100 c. c. of saline, and got the usual great prolongation of dilatation. I then added to the saline 25 c. c. of white-of-egg mixture, composed of one part white of egg in two parts of water. In two minutes the contractions became exactly as they were when the heart was supplied with blood mixture. White of egg consists of albumins and chloride of potassium and sodium, chiefly chloride of potassium. It is obvious in the preceding experiment that the effect of white of egg could not be due to the sodium chloride. The power to obviate the great prolongation of the dilatation occurring when the ventricle was supplied with saline solution must then be due to the albumins or the potassium chloride.

I find that potassium chloride in small quantities, much smaller than exists in serum, will completely and speedily obviate the character of the trace occurring with saline solution, and give a trace in all respects like that occurring when the ventricle is supplied with blood mixture. This is well shown in Fig. 5. I first took a tracing with blood mixture (see A), and then replaced the blood with 100 c. c. of saline solution. After about 15 minutes I obtained the usual great prolongation of the ventricular dilatation (see B).

I then added to the 100 c. c. of circulating saline 0.7 c. c. of 1 per cent. solution of potassium chloride (see C) at the point indicated by the arrow; very speedily the contraction became modified, the dilatation becoming much shorter. Ten minutes after the addition of the potassium chloride the contraction became just like those at the beginning of the experiment when the ventricle was supplied with blood (see D). From numerous experiments I find that from 0.6 c. c. to 1 c. c. of 1 per cent. solution of potassium chloride to the 100 c. c. of saline solution is sufficient to remove the prolongation of dilatation occurring with saline solution.

Like blood mixture small doses of chloride of potassium obviate the changes occurring in the later stages of a ventricle fed with saline solution. This is well seen in Fig. 6. After the trace had become greatly weakened (see C), the dilatation remaining greatly prolonged, I added 1 c. c. of 1 per cent. solution of potassium chloride. This speedily altered the trace; it accelerated the dilatation and brought the whole trace nearer the base line. The contractions then grew slowly stronger, and in 34 minutes they were nearly as good (see G) as at the beginning of the experiment, when the ventricle was supplied with blood (see A). On another occasion I restored good contractions by the addition of 0.7 c. c. of 1 per cent. solution of potassium chloride.

Phosphate of potash in smaller doses than exist in the blood likewise obviates the prolonged relaxation occurring with saline solution. I employed a 1 per cent. solution of potassium phosphate from which the greater part of water of crystallization was driven off by placing the salt over a water bath for two hours at a temperature of 212° Fahr. I found that 0.6 c. c. of this solution greatly and speedily shortened the duration of the dilatation occurring with saline solution, and 1.5 c. c. restored the trace to its condition when the ventricle was supplied with blood.

Phosphate of soda, however, does not remove the prolonged dilatation with saline solution, even with quantities largely in excess of the amount of sodium phosphate in the blood. The effect, then, in potassium phosphate is due to the potassium and not to the phosphoric acid.

Probably any potassium salt is sufficient to obviate the prolonged dilatation occurring when the ventricle is fed with saline solution only, for I have produced normal contractions by adding to the saline solution potassium chloride, potassium phosphate, potassium sulphate, potassium citrate, potassium bicarbonate, potassium chlorate, potassium nitrate, potassium acetate, and potassium carbonate.

With all of these 1 to 2 c. c. of one per cent. solution added to 100 c. c. of saline solution was sufficient to give a normal contraction.

As an illustration of the effect of potassium salts, I describe the following experiment: I first took a trace with blood mixture. I then replaced the blood with saline solution and obtained the saline trace. I then added 1.5 c. c. of potassium chlorate to the saline, and soon the trace became normal, like that with blood mixture. I then again supplied the ventricle with saline solution, and a second time obtained the saline trace, and then I added 1.5 c. c. of 1 per cent. solution of potassium nitrate and produced a normal contraction. I then a third time supplied the heart with saline solution, and a third time produced the saline trace. I then added 1.5 c. c. of 1 per cent. solution of potassium acetate and produced normal beats. I then a fourth time supplied the ventricle with saline, and a fourth time obtained the saline trace. I then added to the saline solution 1 c. c. of 1 per cent. solution of potassium carbonate, and produced normal beats in all respects like those at the commencement of the experiment when the ventricle was supplied with blood mixture.

I next tested the effect of serum albumin, free from potassium salts, on the saline trace. I dialyzed serum of lamb's blood for four days, and dissolved the precipitated albumin by adding to 100 c. c. of the dialyzed serum an equal quantity of  $1\frac{3}{4}$  per cent. of sodium chloride solution, and added 1 c. c. of 1 per cent. solution of bicarbonate of soda. I first took a trace with blood mixture, and then replaced the blood with 100 c. c. of saline solution. The usual great prolongation of dilatation ensued, and I then added to the saline solution 25 c. c. of the serum mixture, but without modifying the trace in the smallest degree. I then added a second 25 c. c. of serum mixture, but still the great prolongation of the ventricular dilatation continued. I then added 1 c. c. of 1 per cent. solution of potassium chloride, and, as usual at first, the contractions grew weaker, but they soon regained their strength and became in all respects like the contraction with blood, the dilatation becoming natural. It is evident, therefore, that the albumin in serum will not obviate the prolonged dilatation that occurs when the ventricle is fed with saline solution alone.

It appears, then, that a small quantity of potassium salt is necessary for the prompt dilatation of the ventricle. It is singular that whilst necessary for the speedy dilatation of the ventricle, potash salts appear less necessary for the proper contraction of the ventricle; for with saline solution the contraction occurs with much the same rapidity as with blood, and the dilatation only is greatly retarded.

I next tested the action of distilled water on the ventricle. I first took a trace with blood mixture, and then replaced this with 100 c. c. of distilled water. Water throws the ventricle into complete and permanent systole; in fact, it affects the cardiac like the skeletal muscles, and induces water rigor. This effect of water is removed by adding sodium chloride to the water. The effects of water, and the counter effect of sodium chloride, are well shown in Fig. 4. A shows the trace with blood mixture. At B is seen the rapid effect of water, the ventricle being thrown into complete and permanent systole. At C is shown the antagonizing effect of sodium chloride, which dilated the ventricle and restored to it spontaneous contractility. After a time the trace presented the usual character with a ventricle fed with saline—that is to say, the dilatation became greatly prolonged. I then added a small quantity of white of egg mixed with water, and in a few seconds the ventricular contractions became just as they were with blood mixture.

Fig. 4a also shows the effect of water and the antagonizing action of sodium chloride.

White of egg dissolved in water affects the ventricle just like water. I diluted white of hen's egg with four times its quantity of water and filtered it. I then took a trace with blood mixture and replaced this with 100 c. c. of the white-of-egg mixture, and produced almost at once complete arrest of the ventricle in complete systole. I then added to the albumin mixture 2 c. c. of 10 per cent. solution of sodium chloride, and in about 70 seconds the heart dilated, and the trace fell to its old position to the base line. Soon after this slight contractions began and increased in strength, the trace again rising higher above the base line—in other words, some tonic spasm set in; soon the trace again fell towards the base line, the tonic spasm ceasing, and then occurred contractions similar to those induced by adding sodium chloride to blood mixture. On replacing the albumin mixture with blood mixture good contractions returned, similar to those at the beginning of the experiment, but the contractions were rather less complete.

We see then that water induces in the ventricle tonic spasm (water rigor), that an addition of white-of-egg albumin will not prevent this, but that the spasm is obviated by sodium chloride.

If some time elapses after the production of water rigor before the addition of sodium chloride solution, then there occurs no return of the beats nor fall in the trace, indeed no effect on the water rigor. I

produced water rigor, and about seventeen minutes after I added 3 c. c. of 20 per cent. sodium chloride solution, and in six minutes another 2 c. c. and continued the observation twenty-two minutes after the first addition of sodium chloride solution, but the water rigor remained unchanged. On another occasion I allowed six minutes to elapse after the induction of water rigor before I added 3 c. c. of 20 per cent. solution The water rigor remained unaffected, though I of sodium chloride. continued the observation eleven minutes after the addition of sodium On another occasion I added 3 c. c. of 20 per cent. solution of sodium chloride to the water 150 seconds (2.5 minutes) after the heart was first supplied with distilled water. This restored feeble contractions, and as usual the trace fell to its natural position to the base line (see Fig. 4a). But the contractions remained very feeble, and then grew weaker and had almost ceased in thirteen minutes after the addition of sodium chloride. I then replaced the water and sodium chloride solution with blood mixture, and in 90 seconds spontaneous contractions began and became very good in nine minutes.

It is evident, therefore, that blood is more efficient in restoring the contractions after water rigor than simple saline solution. But if too long an interval elapses between the production of water rigor and the substitution of the blood mixture for water, the water rigor remains unaffected by the blood. I induced water rigor, eleven minutes after the use of water I replaced it by blood solution, but the water rigor remained unaffected.

We see, therefore, that water, or water and white of egg, first induce spasm—a condition closely similar to rigor mortis—and, after a little while longer, true rigor mortis, the ventricle becoming white and opaque, and then neither sodium chloride nor blood mixture can cause the ventricle to dilate and to resume contractility.

Is the action of simple water on the heart merely physical, and does chloride of sodium simply prevent these physical effects?

To see how far sodium chloride acts merely physically, I used syrup 1.3 in two parts. First I produced water rigor, and then added to the circulating water 1 c. c. and subsequently another c. c. of the syrup without in any degree lessening the water rigor. On another occasion I substituted for the blood mixture 100 c. c. of distilled water, to which I had previously added 3 c. c. of this syrup, but the water rigor occurred in spite of this and was removed by the addition of 3 c. c. of 20 per cent. sodium chloride solution.

Phosphate of soda will, however, remove water rigor. On two

occasions I removed it—the heart fully dilating—with 3 c. c. of 20 per cent. solution added to 100 c. c. of circulating water. In one experiment no contractility returned, either spontaneously or with strong faradaic excitation; on the other occasion, slight and frequent contractions returned, but ceased in about seven minutes, and were not restored by 1 c. c. of potassium chloride 1 per cent. solution, but were by substituting blood mixture.

We see that water produces water rigor, i.e. tonic contraction of the ventricle, and that sodium chloride prevents this effect. But with saline solution while contraction is normal, dilatation is greatly prolonged. Is this slow dilatation of the ventricle due to the effect of water being only partially antagonized by saline solution? If this suggestion is correct the stronger solution of sodium chloride should quicken the dilatation and make it normal. But this is not the case, for I have used solutions containing 1, 1.5, 1.7, and 2 per cent. and yet never obtained a normal trace but the saline trace, the effects occurring much sooner than with 0.7 solution. A stronger solution than 2 per cent. quickly arrests the ventricle in diastole.

I find that potassium chloride in physiological doses does not remove water rigor. I made three experiments, and after the production of water rigor added to the circulating water 1 c. c. of 1 per cent. of potassium chloride without any effect. This indeed one would expect, for white of egg, which contains a fair quantity of potassium chloride, does not prevent water rigor.

I next experimented to learn how far chloride of potassium is able in larger doses to prevent the effects of water (water rigor). When administered with blood, potassium salts are far more poisonous than soda salts. 1.5 c. c. of 10 per cent. solution of potassium chloride added to 100 c. c. of blood mixture quickly arrests the heart in diastole. Again, we have seen the striking effect of a quantity less than that present in the blood on the prolonged dilatation of the ventricle supplied with sodium chloride solution.

Although potassium chloride is powerful in arresting the ventricle in diastole, yet it cannot prevent water rigor. I first took a trace with blood mixture, and then substituted 100 c. c. of distilled water for the blood and quickly produced water rigor. Then, before spontaneous contractions were abolished, I added 3 c. c. of 1 per cent. potassium chloride solution, and in about a minute and a half another 2 c. c., but the ventricle remained firmly contracted and did not beat spontaneously, nor could contractions be induced by a strong induction shock.

On another occasion, after taking a tracing with blood mixture, I replaced it with 100 c. c. of distilled water, to which I had added 5 c. c. of 10 per cent. solution of potassium chloride; but this neither prevented nor retarded the onset of water rigor, and immediately this occurred I added another c. c., and in about a minute 2 c. c. more, but without removing, or even lessening, the contraction of the ventricle. I then replaced the potassium chloride solution with blood and the ventricle soon dilated, and the trace fell to the base line, and shortly after this good spontaneous beats returned. I replaced the blood with 100 c. c. of water, to which I had added 5 c. c. of 10 per cent. solution of potassium chloride; but again water rigor speedily set in as complete as with water alone. Immediately the ventricle became quite contracted. added another 5 c. c. of 10 per cent. solution, but did not at all lessen the contraction. I then replaced the potassium chloride solution by 100 c. c. of 0.75 per cent. solution of sodium chloride solution, and the ventricle quickly dilated, the trace falling to the base line, and soon good contractions ensued. I then added to the saline solution 2 c. c. of 10 per cent. solution of potassium chloride, and in a few seconds the ventricle became arrested with some persistent spasm, which, however, soon disappeared (see Fig. 7).

On another occasion, after taking a trace with blood mixture, I substituted for the blood 100 c. c. of 0.75 per cent. solution of potassium chloride, and threw the ventricle into strong systole, which persisted six minutes, when I replaced the chloride of potassium solution by blood. In about 3 minutes contractions returned, and when these had become fair I again replaced the blood by potassium chloride 0.75 per cent. solution, and this time the contractions grew rapidly weaker and the ventricle stopped beating in diastole.

At another time after a blood trace I replaced the blood by 0.75 per cent. solution of potassium chloride. I produced partial systole, and the trace fell towards the base line, but remained higher than with blood. I replaced the potassium chloride solution by blood and got back contractions, and again replaced the blood by 0.75 per cent. solution of potassium chloride. The contractions grew less and less complete and the ventricle stopped in diastole; but immediately after the ventricle slowly contracted again and passed into a state of persistent spasm. I again restored spontaneous beats by means of blood mixture, and again replaced the blood by 100 c. c. of 0.75 per cent. solution of potassium chloride and again obtained the same result, the beats growing weaker and the ventricle stopping in diastole, but then slowly passing into persistent spasm.

It appears, then, that neither physiological nor toxic doses of potassium chloride will obviate the contraction induced by water.

Part of the persistent contraction of these last experiments is probably due to the potassium chloride, for though with the addition of small doses at a time, the ventricle becomes arrested in diastole without the production of any persistent spasm, yet if a large dose be added at once the contractions grow weak or are arrested, and then occurs a considerable amount of persistent contraction, which, however, speedily declines.

We see, then, that water alone induces persistent spasm, and that this is not prevented by potassium chloride nor by albumin (white of egg), but is obviated by sodium chloride. Sodium chloride solution alone, however, is accompanied by considerable prolongation of the dilatation of the ventricle, so that, with the heart beating at its normal frequency, there would occur a considerable amount of fusion of the beats, and the heart's work would be considerably interfered with. Minute doses of potassium salts, smaller even than exist in the blood, when added to the saline solution greatly accelerate the dilatation of the ventricle and give a normal beat in all respects similar to that produced by blood.

As might be expected from the preceding experiments, I find that saline solution, to which is added one ten-thousandth part of potassium chloride, makes an excellent circulating fluid in experiments with the detached heart.

On May 31, with the temperature of the room 17.5 C., I first took a tracing with blood mixture, and then replaced this with 100 c. c. saline solution, to which I had added 1 c. c. of 1 per cent. solution of potassium chloride. The contractions continued quite unaltered, and complete contractions still persisted an hour after the heart was first supplied with the saline and potassium mixture. On another occasion, after taking a trace with blood mixture, I substituted for the blood saline solution with 1 c. c. of 1 per cent. solution of potassium chloride solution. The contractions retained the same character, and at the end of four hours and a half were almost as good as at the beginning of the experiment. On another occasion I used sulphate of potash, adding 1 c. c. of 1 per cent. solution to 100 c. c. of saline. This in no way changed the character of the contractions from those occurring with blood mixture, and at the end of four hours and a half the contractions were only very slightly weaker than at the commencement of the experiment.

## EXPLANATION OF PLATES.

## Fig. O.

- A. Trace with blood mixture.
- B. Twelve minutes after saline solution was substituted for blood mixture.
- C. Twenty minutes after saline solution substituted for blood mixture.
- D. Thirty-three minutes after saline solution was substituted for blood mixture.
- E. From another experiment. Thirty-six minutes after saline solution was substituted for blood mixture.
- F. Sixty-five minutes after saline solution substituted for blood mixture.
- G. See Text.
- H. See Text.
- I. See Text.

## Fig. Oa.

# Trace with quicker rate.

- A. Trace with blood mixture.
- B. Taken about half-an-hour after saline solution was substituted for blood mixture.

#### Fig. 1.

- A. Trace with blood mixture.
- B. Trace when saline solution was substituted for blood mixture.
- C. Showing partial tetanus by fusion of the beats, owing to great prolongation of the contractions.

#### Fig. 2.

Showing the effect of blood mixture on the saline trace.

At the point indicated by the arrow 50 c. c. of blood mixture were added to the circulating saline, and the contractions speedily became less frequent and weaker, and of shorter duration. In a short time good normal contractions returned.

## Fig. 2A.

- A. Trace with blood mixture.
- B. Sixty-three minutes after saline solution substituted for blood mixture.
- C. About six minutes after saline solution replaced by blood mixture.
- D. Forty-two minutes after saline solution was replaced by blood mixture.

#### Fig. 3.

- A. Effect of 5 c. c. of 20 per cent. solution of sodium chloride added to 100 c. c. of blood mixture. Sodium chloride solution added at the place indicated by an arrow.
- B. Trace after the addition of 50 c. c. of water to the circulating fluid and the subsequent addition of 2 c. c. of sodium chloride solution 20 per cent.
- C and D. After the substitution of saline solution for blood mixture.

## Fig. 3A.

Showing the effect of adding a strong solution of sodium chloride to blood mixture.

- A. Trace with blood mixture alone.
- B. After the addition of 6 c. c. of 10 per cent. solution of sodium chloride.
- C. After the addition of 9 c. c. of sodium chloride solution.
- D. After the addition of 12 c.c. of sodium chloride solution.
- E. After the addition of 14 c. c. of sodium chloride solution.

## Fig. 4.

Showing the effect of water on the ventricle and the antagonizing effect of sodium chloride.

- A. Tracing with blood mixture.
- B. After substituting water for blood mixture. The arrow indicates the time water was substituted for blood.
- C. After the addition of 2 c. c. of 20 per cent. solution of sodium chloride.

  The arrow indicates the time the sodium chloride solution was added to the circulating water.
- D. Effect of further addition of 1 c. c. of 20 per cent. solution of sodium chloride.
- E. Later effect.
- F. Effect of another c. c. of 20 per cent. solution of chloride of sodium, 4 c. c. in all, to the 100 c. c. of water. The trace well shows the effect of sodium chloride solution in prolonging dilatation.
- G. Effect of 25 c. c. of white of egg mixture. One part of white of egg to two parts of water.

#### Fig. 4A.

- A. Shows the trace with blood mixture, and the effect of replacing this with 100 c. c. of distilled water, and the effect of adding 3 c. c. of 20 per cent. solution of sodium chloride. The water was substituted at a, and the sodium chloride solution was added at b.
- B. Eleven minutes after the addition of sodium chloride.

- C. Thirteen minutes after the addition of sodium chloride solution. I then replaced the water and saline by blood mixture.
- D. Nine minutes after, substituting blood mixture for the water and saline.

## Fig. 5.

Shows the effect of physiological doses on the saline trace.

- A. Trace taken with blood mixture.
- B. Fifteen minutes after blood mixture was replaced by saline solution.
- C. Effect of adding 0.7 c. c. of 1 per cent. solution of potassium chloride to the 100 c. c. of circulating saline solution. The arrow indicates the time the potassium chloride was added.
- D. Effect ten minutes later.

## Fig. 6.

Shows the effect of physiological doses of potassium chloride on the later stages of the saline solution trace. All the contractions were excited by faradic shocks.

- A. Trace with blood mixture.
- B. Thirty-three minutes after substituting saline solution for blood mixture.
- C. One hundred and ten minutes after substituting saline solution for blood mixture.
- D. Immediate effect of adding to the 100 c. c. of circulating saline solution 1 c. c. of 1 per cent. solution of potassium chloride.
- E. Eleven minutes after the addition of potassium chloride.
- F. Twenty-two minutes after the addition of potassium chloride.
- G. Thirty-four minutes after the addition of potassium chloride.

## Fig. 7.

Showing the effect of potassium chloride solution.

- A. Blood replaced at first arrow by 100 c. c. distilled water containing 5 c. c. of 10 per cent. solution of potassium chloride.
  - Another c. c. of potassium chloride solution added at second arrow.

    Two c. c. of potassium chloride solution (10 per cent.) added at third arrow.
- B. Shows the effect of substituting blood solution for potassium chloride solution. Blood mixture substituted at arrow.
- C. Shows effect of again substituting potassium chloride solution for blood mixture. At first arrow 100 c. c. of water containing 5 c. c. of 10 per cent. solution of potassium solution substituted for blood mixture. At second arrow added 5 c. c. of 10 per cent. solution of potassium chloride. At third arrow substituted saline solution for potassium chloride solution.
- Shows the effect of 100 c. c. saline containing 2 c. c. of 10 per cent. solution of potassium chloride. This mixture substituted at arrow.
   PH. III.